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AMENDMENT		
Address to: Assistant Commissioner for Patents Washington, D.C. 20231	Attorney Docket Confirmation No.	CLON015
	First Named Inventor	Chenchik et al.
	Application Number	09/440,829
	Filing Date	November 15, 1999
	Group Art Unit	1655
	Examiner Name	Forman, B.
	Title	*Long Oligonucleotide Arrays*

Sir:

This amendment is submitted in response to the FINAL REJECTION dated August 3, 2001.

Please amend the above identified application as follows:

IN THE CLAIMS:

1. (Twice Amended) An array comprising at least one pattern of probe oligonucleotide spots stably attached to the surface of a solid support, wherein each probe oligonucleotide spot of said pattern comprises an oligonucleotide probe composition made up of long oligonucleotide probes that range in length from about 50 to 100 nucleotides.

36. (Once Amended) The array according to Claim 1, wherein any variance in hybridization efficiency among any two probes of said array does not exceed about 10-fold.

37. (Once Amended) The array according to Claim 14, wherein any variance in

hybridization efficiency among any two probes of said array does not exceed about 10-fold.

38. (Once Amended) The array according to Claim 23, wherein any variance in hybridization efficiency among any two probes of said array does not exceed about 10-fold.

REMARKS

In view of the above amendments and the following remarks, the Examiner is respectfully requested to withdraw the rejections and allow Claims 1-3, 7-23 and 35-38, the only claims pending and currently under examination in this application.

Claim 1 has been amended to clarify the association of the probes to the substrate surface and also to further narrow the scope of the base length range. In addition, Claims 35 to 38 have been amended to correct a typographical error in the original claim language. As the above amendments introduce no new matter to the application, their entry by the Examiner is respectfully requested.

Attached hereto is a marked up version of the changes made to the claims by the current amendment. The attached page is captioned **"Version with markings to show changes made."**

Claims 36 to 38 were rejected under 35 U.S.C. §112, 2nd ¶ for "omitting essential elements," such as a description in hybridization efficiency and variance thereof, as well as a description of which probes are measured. In view of the above amendments, the claims are now clear that it is any two probes on the array that meet the hybridization efficiency parameter. Furthermore, in view of the specification and working exemplification, as well as the previously submitted 1.132 declaration submitted by Dr. Chenchik, one of skill in the art would clearly know what the terms "hybridization efficiency" refer to in the claims and how a variance of this

value is determined. As such, the claim language is clear in view of the specification and this rejection may be withdrawn.

Claims 1-3 & 10-22 have been rejected under 35 U.S.C. § 103(a) as asserted being obvious over Brown et al. in view of Bresser et al. In making this rejection, the Examiner acknowledges that Brown does not specifically teach the claimed narrow range of 50 to 100 nt in length but just makes the broad teaching of over 50. However, the Examiner asserts that since Bresser discloses that the probes in Bressers disclosed assay are 50 to 150 bases in length, the claims are obvious over the combined teachings of these references, as one would be motivated to modify Browns lengths to be between 50 to 150 bases to enjoy the benefits taught by Bresser.

However, Bresser does not disclose an array of nucleic acid probes or assays using the same. Instead, Bresser describes an *in situ* hybridization protocol, where total RNA from cells/tissues (i.e., target) is immobilized on solid surface and hybridization probes corresponding unique genes are present in solution. While the size of probes is taught to be between 50 and 150 bases, **this teaching is for probes in solution**, not for probes attached to a solid surface. As such, Bresser is concerned with a completely different system than arrays and is not concerned with probe nucleic acids that are attached to a surface. Instead, Bresser is only concerned with probes nucleic acids in solution.

The Examiner has provided no evidence that probes in solution act the same as probes attached to a solid support. Furthermore, one would expect these two different types of probes to act differently, because the probe on the support is necessarily constrained in movement while the probe in solution may move freely. Without evidentiary support showing that probes in solution act the same as probes attached to a solid support, one cannot extrapolate what is taught to be beneficial for probes in solution to what is beneficial for probes attached to a solid support.

As such, one would not apply the teaching of Bresser to modify Brown's arrays to arrive at the claimed invention because the benefits taught by Bresser of using probes of 50 to 150 bases in length in a non-array hybridization protocol where the probes are in solution can not be extrapolated to probes affixed to a solid support.

Furthermore, as pointed out in the Applicants prior response, the Applicants have found unexpected results when using probes of the claimed narrow ranges, as demonstrated by the previously filed Declaration and reported in the Experimental Section of the application as Example 6. The Examiner attempts to discount this evidence stating that it is unpersuasive because it does not show what happens for probes that are less than 50 or greater than 100 bases in length. However, the previously submitted declaration shows the results that would have been expected for probes of the claimed ranges and what was observed for the probes of claimed range, and concludes that what was observed differed from what was expected in an unexpected manner. There is no need to provide evidence of less than 50 or greater than 100 to demonstrate unexpected results as such has already been demonstrated by showing what was expected for the claimed range and what was actually observed for the claimed range.

Because: (a) Brown fails to suggest the narrowly claimed range of the instant claims and Bresser's teaching would not motivate one to modify Brown to use the claimed range because Bresser is concerned with a non-array system and probes in solution, not affixed to a solid support; and (b) the Applicants have demonstrated unexpected results using the claimed range, Claims 1-3 and 10-22 are not obvious under 35 U.S.C. § 103(a) over Brown in view of Bresser and this rejection may be withdrawn.

Claims 7 and 23 have been rejected under 35 U.S.C. §103(a) as obvious over Brown and Bresser in view of Chetverin. As demonstrated above, the combined teaching of Brown and Bresser fails to teach or suggest the claimed narrow length range of the present claims. As Chetverin has been cited solely for its teaching of covalent attachment of the probes to the solid

support, Chetverin fails to make up this fundamental deficiency in the combined teaching of Brown and Bresser. As such, Claims 7 and 23 are not obvious over the combined teaching of Brown and Bresser in view of Chetverin and this rejection may be withdrawn.

Claims 8 and 9 have been rejected under 35 U.S.C. §103(a) as obvious over Brown and Bresser in view of Chetverin and further in view of Graves. As demonstrated above, the combined teaching of Brown and Bresser fails to teach the narrow claimed range of oligonucleotide length. Furthermore, the narrow claimed range provides for unexpected results. As such, the narrow claimed range is not obvious over the combined teaching of Brown and Bresser. As Chetverin has been cited solely for its teaching of covalent attachment of the probes to the solid support and Graves has been cited solely for its teaching of cross-linking, these supplemental references fail to make up this fundamental deficiency in Brown and Bresser. As such, Claims 8 and 9 are not obvious over the combined teaching of Brown and Bresser in view of Chetverin and Graves and this rejection may be withdrawn.

Claims 36 and 37 has been rejected under 35 U.S.C. §103(a) as obvious over Brown and Bresser. As demonstrated above, the combined teaching of Brown and Bresser fails to teach the narrow claimed range of oligonucleotide length. Furthermore, the narrow claimed range provides for unexpected results. As such, the narrow claimed range is not obvious over the Brown/Bresser combined disclosure. As such, Claims 36 and 37 are not obvious over the combined teaching of Brown and Bresser and this rejection may be withdrawn.

Claim 38 has been rejected under 35 U.S.C. §103(a) as obvious over Brown and Bresser in view of Chetverin. As demonstrated above, the combined teaching of Brown and Bresser fails to teach the narrow claimed range of oligonucleotide length. Furthermore, the narrow claimed range provides for unexpected results. As such, the narrow claimed range is not obvious over the Brown/Bresser combined disclosure. As Chetverin has been cited solely for its teaching of covalent attachment of the probes to the solid support, it fails to make up this fundamental

deficiency in Brown/Bresser. As such, Claim 38 is not obvious over the combined teaching of Brown and Bresser in view of Chetverin and this rejection may be withdrawn.

In view of the above amendments and remarks, this application is considered to be in good and proper form for allowance and the Examiner is respectfully requested to pass this application to issuance. The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815.

Respectfully submitted,
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Date: November 5, 2001

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